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June 11, 2024

The Honorable Richard G. Andrews
United States District Court
for the District of Delaware
J. Caleb Boggs Federal Building
844 North King Street
Room 6325, Unit 9
Wilmington, DE 19801-3555

VIA ELECTRONIC FILING

Re: **Request for Leave to File Motion for Summary Judgment**
San Rocco Therapeutics, LLC v. bluebird bio, Inc., et al.,
C.A. No. 21-1478 (RGA)

Dear Judge Andrews:

For the reasons below, Defendants respectfully request leave to file a case-dispositive motion for summary judgment that Defendants do not infringe any asserted claim of the patents-in-suit,[1] including under the doctrine of equivalents, because Plaintiff San Rocco Therapeutics, LLC ("SRT") is precluded from relying on that doctrine as a matter of law.

I. SRT Admits That BB305 Does Not Literally Infringe the Asserted Claims

Applying the Court's recent construction of "consists essentially of" (D.I. 168 at 5), BB305, the accused instrumentality in this case, does not contain a "3.2-kb nucleotide fragment which consists essentially of three continuous nucleotide fragments obtainable from a human β-globin locus control region (LCR)." BB305 incorporates a 2.7 kb LCR (*see* D.I. 141 at 9-10)—a 500-bp difference between the LCR of BB305 and the LCR claimed in the patents-in-suit.

[1] SRT has alleged that Defendants infringe claims 1, 10, 19, 22-24 of the '179 patent and claims 1-3, 5-8, 11-12, and 15 of the '061 patent.

Further, each of BB305's HS fragments are different from the "HS2," "HS3," and "HS4" fragments claimed in the patents-in-suit:[2]

- The claimed HS2-spanning fragment is "located at nucleotides 8055-8911 and has a size of 857 bp" (D.I. 168 at 12), while the HS2 of BB305 is located at nucleotides 8225-8863 and has a size of 644 bp (*see* D.I. 147 at JA1421-22; D.I. 141 at 10 n.8.)

- The claimed HS3-spanning fragment is "located at nucleotides 3878-5172 and has a size of 1295 bp" (D.I. 168 at 12), while the HS3 of BB305 is located at nucleotides 4279-5125 and has a size of 845 bp (*see* D.I. 147 at JA1421-22; D.I. 141 at 10 n.8.)

- The claimed HS4-spanning fragment is "located at nucleotides 308-1388 and has a size of 1081 bp" (D.I. 168 at 12), while the HS4 of BB305 is located at nucleotides 559-1712 and has a size of 1153 bp (*see* D.I. 147 at JA1421-22; D.I. 141 at 10 n.8.)

As it must, SRT now concedes that BB305 does not literally infringe any asserted claim of the patents-in-suit. (*See* Ex. A, May 30, 2024 e-mail from W. French-Brown.)

II. SRT Is Precluded from Relying on the Doctrine of Equivalents

The narrow, targeted claims of the patents-in-suit came about as a result of a need to overcome prior art and Section 112 rejections during prosecution of the patents-in-suit. Governing law forecloses SRT from now arguing that the (at least) four missing claim limitations of each asserted claim are present in BB305 by equivalence.[3] Defendants therefore respectfully seek leave to confirm via summary judgment that SRT is precluded from relying on the doctrine of equivalents because of (1) amendment-based prosecution history estoppel, (2) argument-based prosecution history estoppel, and (3) claim vitiation.[4] This is a legal issue that can be resolved on

[2] For efficiency, Defendants have focused on the limitations of the asserted independent claims. SRT additionally cannot show that limitations of the asserted dependent claims are met by BB305, though the Court need not decide that issue to dispose of this action.

[3] The doctrine of equivalents is applied on a limitation-by-limitation basis. *See, e.g.*, *Warner-Jenkinson Co. v. Hilton Davis Chemical*, 520 U.S. 17, 29 (1997) ("Each element contained in a patent claim is deemed material to defining the scope of the patented invention, and thus the doctrine of equivalents must be applied to individual elements of the claim, not to the invention as a whole.").

[4] SRT cannot meet its affirmative burden to show that the claim limitations missing for literal infringement are otherwise present by equivalent in BB305 because of any alleged "insubstantial differences," or under the "function-way-result" test, including based on its own expert's testimony in the IPR proceedings that "a POSA would understand that something as small as 1 bp or even up to 100 bp could be the difference between the vector working or not working." (D.I. 147 at JA0747.) The LCR incorporated in BB305 differs from that claimed in the patents-in-suit

the intrinsic record—the same record that the Court has just considered as part of the *Markman* proceedings—without the need for expert testimony and without any genuine dispute as to any material fact. Resolution of noninfringement now would maximize efficiency given the overlap with the issues just considered by the Court and conserve substantial resources for the parties and the Court in obviating the need for further fact discovery, expert discovery, and trial.

a. SRT Is Estopped from Recapturing BB305 Through the Doctrine of Equivalents Due to Amendment-Based Prosecution History Estoppel

When a patentee narrows its claims via amendment during patent prosecution, it is estopped from recapturing the forfeited claim scope through the doctrine of equivalents. *See Festo Corp. v. Shoketsu Kinzoku Kogyo Kabushiki Co.*, 535 U.S. 722, 724 (2002) ("Estoppel arises when an amendment is made to secure the patent and the amendment narrows the patent's scope."). The prosecution record here is clear: The patentee surrendered claims to a vector with "large portions of the β-globin locus control region" in favor of claims with specific limitations as to the LCR length and the HS fragments to overcome examiner rejections. This presumptively estops SRT from arguing that these same limitations are met by equivalence. *See, e.g.*, *id.*, 535 U.S. at 737; *Pioneer Magnetics, Inc. v. Micro Linear Corp.*, 330 F.3d 1352, 1356 (Fed. Cir. 2003).

The originally filed first independent claim of the application issuing as the '179 patent was broadly directed to "[a] recombinant lentiviral vector comprising: (a) a region comprising a functional globin gene; and (b) large portions of the β-globin locus control region, which include DNase hypersensitive sites HS2, HS3 and HS4, said vector providing expression of the globin gene when introduced into a mammal *in vivo*." (D.I. 146 at JA0076.) The pending claims were rejected on both prior art and Section 112 grounds. For example, the examiner concluded that "[i]t is well-established in the prior art of record that recombinant viral vectors comprising more than the [1 kb] core portions [of] the β-globin locus control region could be routinely made to drive expression of the human beta-globin gene when introduced into a mammal *in vivo*," citing a number of different publications teaching vectors incorporating β-globin LCR's made up of different HS2, HS3, and HS4 fragments. (*Id.* at JA0137-45 (emphasis in original).) As a result, the Examiner expressly recommended narrowing the claim limitations to "obviate" the outstanding rejections. (D.I. 146 at JA0137.)

On June 30, 2005, the patentee amended the claims as suggested by the examiner, and further amended the claims on September 12, 2007, as shown below (narrowing limitations shown in red):

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by hundreds of nucleotides. The Court, however, need not reach these issues, as SRT is foreclosed from relying upon the doctrine of equivalents as a matter of law for the reasons described herein.

Originally Filed Claim 1 (July 1, 2002) (D.I. 146 at JA0076)	**Amended Claim 1 (September 12, 2007)** (D.I. 146 at JA0249; *see also* JA0155 (June 30, 2005 Amendments)
1. A recombinant lentiviral vector comprising: (a) a region comprising a functional globin gene; and (b) large portions of the β-globin locus control region, which include DNase I hypersensitive sites HS2, HS3, and HS4, said vector providing expression of the globin gene when introduced into a mammal in vivo.	1. A recombinant vector comprising: (a) a region comprising a nucleotide sequence encoding a functional globin; and (b) a 3.2-kb portion of a β-globin locus control region (LCR) which consists essentially of an HS2-spanning nucleotide fragment extending between BTXI and SnaBI restriction sites of said LCR, an HS3-spanning nucleotide fragment extending between BamHI and HindIII restriction sites of said LCR and an HS4-spanning nucleotide fragment extending between BamHI and BanII restriction sites of said LCR, said vector providing expression of globin when introduced into a mammal *in vivo*.

Having narrowed the claims to a specific 3.2-kb LCR made up HS2, HS3, and HS4 fragments having precise sizes, SRT is estopped from arguing that those same limitations are met by equivalence. *See Festo Corp.*, 535 U.S. at 736.

SRT cannot overcome the presumption of estoppel via any of the three narrow exceptions identified by the Supreme Court in *Festo*. *See Integrated Tech. Corp. v. Rudolph Techs., Inc.*, 734 F.3d 1352, 1356 ("A patentee bears the burden to rebut the presumptive application of prosecution history estoppel by establishing one of three exceptions by a preponderance of the evidence."). Specifically, SRT cannot show that: (1) the alleged equivalent was unforeseeable at the time of the amendment; (2) the rationale underlying the narrowing amendment bore no more than a tangential relation to the equivalent in question; or (3) any other reason suggests that the patentee could not have reasonably been expected to describe the equivalent. *See id.* (citing *Festo Corp.*, 535 U.S. at 740-41).

First, the LCR length and HS fragment sizes of BB305 were foreseeable at the time of application. As explained during the *Markman* proceeding, the HS3 and HS4 fragments used to make the LCR of BB305 were discussed in a 1997 publication from Dr. James Ellis, and the ***exact*** LCR incorporated into BB305 (including the specific HS2, HS3, HS4 fragments) wase described in a 2001 publication by Dr. Robert Pawliuk and colleagues. (*See* D.I. 141 at 10 (citing D.I. 149 at JA0457 (Ellis) and JA0435 (Pawliuk); Markman Tr. at 17:12-18:4; Defendants' Claim Construction Presentation at 2.) Accordingly, the distinct LCR length and specific HS2, HS3, and HS4 fragments found in BB305 were plainly foreseeable as of the earliest June 2005 narrowing amendment (and subsequent further narrowing amendments), and may not be recaptured through the doctrine of equivalents. *See Festo Corp. v. Shoketsu Kinzoku Kogyo Kabushiki Co.*, 344 F.3d

1359, 1365 n.2 (Fed. Cir. 2003) (clarifying on remand that "the time when the narrowing amendment was made . . . is the relevant time for evaluating unforeseeability"); *Schwarz Pharma, Inc. v. Paddock Lab's., Inc.*, 504 F.3d 1371, 1377 (Fed. Cir. 2007) (affirming district court's grant of summary judgment of noninfringement where alleged equivalent "was known . . . by those of skill in the art at the time of the amendment").

Second, the patentee's narrowing amendments bear more than "a tangential relation to the equivalent[s] in question." *Festo Corp.*, 535 U.S. at 740-41; *see also Pharma Tech Sols., Inc. v. LifeScan, Inc.*, 942 F.3d 1372, 1379 (Fed. Cir. 2019) (affirming district court grant of summary judgment of noninfringement due to prosecution history estoppel and explaining that the "tangential relation" analysis "focuses on the patentee's objectively apparent reason for the narrowing amendment, which should be discernible from the prosecution history record"). As discussed above, the patentee's narrowing amendments here were objectively made to overcome the size and makeup of LCR regions disclosed in the prior art, which the examiner noted "well-established . . . that recombinant vectors comprising ***more than*** ***the [1 kb] core portions [of] the ß-globin locus control region*** could be routinely made to drive expression of the human beta-globin gene when introduced into a mammal *in vivo*." (D.I. 146 at JA0137 (Mar. 31, 2005 Rejection) (emphasis added)). The patentee confirmed the importance of the narrow LCR length and HS fragments claimed, stating: "recombinant vectors comprising ***this specific assembly*** of three recited LCR fragments (*i.e.*, a 3.2-kb nucleotide fragment consisting essentially of the three specified fragments—as well as encoding a functional globin) define the scope of the invention, whereas any vector lacking the claimed 3.2-kb fragment with the three LCR fragments assembled in a contiguous manner is excluded from the scope of the claimed subject matter."). (D.I. 146 at JA0379-80 (emphasis added).)

Third, no "other" reason could rebut the presumption of estoppel here. Any "other reason must be such that the patentee could not reasonably be expected to write a claim to encompass the equivalent, such as a shortcoming of language." *Amgen Inc. v. Hoechst Marion Roussel, Inc.*, 457 F.3d 1293, 1316 (Fed. Cir. 2006) (internal quotations and citations omitted). No "other" reason is applicable here, where the patentee attempted to obtain broad claims that could have "encompass[e]d the equivalent" limitations, and where those same LCR length and HS fragments that SRT would argue are met by equivalence were described in the prior art. Prosecution history estoppel applies here, and precludes SRT from alleging infringement under the doctrine of equivalents.[5] *See id.; Pioneer Magnetics, Inc.*, 330 F.3d at 1356 (Federal Circuit affirming grant

[5] SRT is likewise estopped from alleging infringement of the asserted claims of the '061 patent, which was filed as a divisional of the '179 patent and includes the same narrowing LCR length and HS fragment limitations that arose during prosecution of the parent application. *Elkay Mfg. Co. v. Ebco Mfg. Co.*, 192 F.3d 973, 980 (Fed. Cir. 1999) ("When multiple patents derive from the same initial application, the prosecution history regarding a claim limitation in any patent that has issued applies with equal force to subsequently issued patents that contain the same claim limitation."); *Silvergate Pharms., Inc. v. Bionpharma Inc.*, 2021 WL 1751148, at *26 (D. Del. Apr. 29, 2021) ("Because each of the Asserted Patents derives priority from one common application, they necessarily share the same prosecution history. To Bionpharma, therefore, the prosecution

of summary judgment of noninfringement where, "given the equivalent's presence in the prior art . . . there can be no other reason the patentee could not have described the substitute in question").

b. SRT Is Estopped from Recapturing BB305 Through the Doctrine of Equivalents Due to Argument-Based Prosecution History Estoppel

SRT is likewise legally estopped from relying on the doctrine of equivalents due to argument-based prosecution history estoppel.[6] The Federal Circuit has confirmed that "[c]lear assertions made during prosecution in support of patentability, whether or not actually required to secure allowance of the claim, may also create an estoppel . . . . The relevant inquiry is whether a competitor would reasonably believe that the applicant had surrendered the relevant subject matter." *Amgen Inc. v. Coherus BioSciences Inc.*, 931 F.3d 1154, 1159 (Fed. Cir. 2019) (quoting *Deering Precision Instruments, L.L.C. v. Vector Distribution Sys., Inc.*, 357 F.3d 1314, 1326 (Fed. Cir. 2003)); *see also Canton Bio Medical, Inc., v. Integrated Liner Techs., Inc.*, 216 F.3d 1367, 1372 (granting summary judgment that patentee was estopped from alleging infringement under doctrine of equivalents where patentee "argued that its invention was a 'particular primer solution,' distinguished by its use of these three specific components from the extensive cited prior art").

In connection with the narrowing amendments discussed above, the patentee time-and-again emphasized the narrowness of the claims and the importance of the 3.2 kb LCR, including its specific HS2, HS3, and HS4 fragments. The patentee made at least the following exemplary representations to the Patent Office during prosecution of the '179 patent:

- "[R]ecombinant vectors comprising this specific assembly of the three recited LCR fragments (*i.e.*, a 3.2-kb nucleotide fragment consisting essentially of the three specified fragments—as well as encoding a functional globin) define the scope of the invention, whereas any vector lacking the claimed 3.2-kb fragment with the three LCR fragments assembled in a contiguous manner is excluded from the scope of the claimed subject matter." (D.I. 146 at JA0379-80 (Dec. 3, 2008 Applicant Remarks).)

- "The simple fact that the combination of the three HS-spanning fragments is 3.2 kb partially (and significantly) closes this aspect of the present claim, qualifies its size

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history of the application that became the '008 patent is representative of each asserted patent; and because, in Bionharma's view, prosecution history estoppel attaches to the '008 patent, it attaches to each of the Asserted Patents . . . . Bionpharma is correct.").

[6] Argument-based prosecution history estoppel is applied to properly construed claims, and is a distinct doctrine from the use of the prosecution history to construe disputed claim terms. *See E.I. du Pont de Nemours & Co. v. Phillips Petroleum Co.*, 849 F.2d 1430, 1438 (Fed. Cir. 1988) ("Using the prosecution history [to construe claim terms] is different from prosecution history estoppel, which is applied as a limitation upon the doctrine of equivalents after the claims have been properly interpreted.").

> and thus provides the boundaries for ascertaining the elements excluded by use of 'consisting essentially of' as the transitional phrase . . . . As Applicants have exhaustively established on the record, the combined size of the three HS-spanning fragments so closely approximates 3.2 kb, that the number of additional nucleotides that could be added to (or removed from) this fragment is relatively few and non-material." (*Id.* at 380 (Dec. 3, 2008 Applicant Remarks).)

- "[T]he claimed LCR is assembled from three restriction fragments with an overall size of 3.2 kb (as now recited in Claim 1), so that one can unambiguously determine the scope of the claimed invention." (*Id.* at JA0256 (Sept. 12, 2007 Applicant Remarks).)

Echoing the patentee, SRT itself reaffirmed the narrow scope of the claims during the *inter partes* review proceeding before the United States Patent & Trademark Office, representing: "After all, the true breakthrough of the invention was . . . developing a groundbreaking expression vector system that employed the correct size of LCR hypersensitive regions—not too big and not too small . . . . It was this 'Goldilocks' approach in determining the right size of LCR fragments in developing a reproducible expression system of globin genes that set the invention apart from prior art efforts." (D.I. 147 at JA0888.)

The plain statements made during prosecution estop SRT from recapturing BB305 via the doctrine of equivalents. The patentee was unambiguous: "any vector lacking the claimed 3.2-kb fragment with the three LCR fragments assembled in a contiguous manner ***is excluded from the scope of the claimed subject matter***." (D.I. 146 at JA0379-80 (Dec. 3, 2008 Applicant Remarks).) BB305 lacks the claimed 3.2 kb LCR, as well as the claimed HS2, HS3, and HS4 fragments, and SRT cannot recapture the claim scope expressly surrendered during prosecution of the '179 patent by equivalence.[7] *See Canton Bio Medical, Inc.*, 216 F.3d at 1372 ("In response to the examiner's rejection Canton argued that its invention was a 'particular primer solution,' distinguished by its use of these three specific components from the extensive cited prior art that included the ILT primer compound. In consideration of this argument, the examiner withdrew the rejection . . . . Canton is estopped from now reaching ILT's prior art primer under the doctrine of equivalents."); *Amgen Inc. v. Coherus BioSciences Inc.*, 931 F.3d 1154, 1160 ("We hold that argument-based prosecution history estoppel applies here because Amgen clearly and unmistakably surrendered unclaimed salt combinations during prosecution.").

c. Claim Vitiation Precludes SRT from Relying on the Doctrine of Equivalents

Beyond estoppel, at least four limitations of the properly construed claims would be vitiated were SRT permitted to argue that BB305 infringes the '179 and '061 patents under the doctrine of equivalents. Claim vitiation, or "the 'all limitations rule' restricts the doctrine of

[7] The argument-based estoppel applies with equal force against the '061 patent. *See, e.g., Elkay Mfg. Co.*, 192 F.3d at 980.

equivalents by preventing its application when doing so would vitiate a claim limitation." *Carnegie Mellon Univ. v. Hoffman-La Roche Inc.*, 541 F.3d 1115, 1129 (affirming "that the district court properly granted summary judgment of noninfringement under the doctrine of equivalents").

Expanding the LCR length and HS2, HS3, and HS4 fragment limitations, present in each and every asserted claim, to encompass BB305 would "render[] the pertinent limitation[s] meaningless." *Id.* *Carnegie Mellon* is instructive, as the Federal Circuit held in affirming the district court's grant of summary judgment of noninfringement under the doctrine of equivalents:

> We agree with Roche and the district court that a finding that *Taq* [the bacterial source in the accused product] is an equivalent of *E. coli* [the bacterial source recited in the claims] would essentially render the "bacterial source [is] *E. coli*" claim limitation meaningless, and would thus vitiate that limitation of the claims. Indeed, in drafting the claims, the patentees specifically chose to limit claim 4 to a recombinant plasmid where the bacterial source is *E. coli*. Appellants cannot now argue that any bacterial source, including *Taq*, would infringe that claim. Accordingly, summary judgment of noninfringement was appropriate.

Carnegie Mellon, 541 F.3d at 1129. Permitting the asserted claims of the patents-in-suit to cover a vector of a different length and with different HS fragments would render meaningless and vitiate those same intentionally inserted limitations. SRT is therefore foreclosed from relying upon the doctrine of equivalents for this independent reason.

* * *

The doctrine of equivalents is a limited one. As the Federal Circuit has "emphasized, . . . the doctrine of equivalents is the exception . . . not the rule, and not merely the second prong of every infringement charge, regularly available to extend protection beyond the scope of the claims." *Eli Lilly & Co. v. Hospira, Inc.*, 933 F.3d 1320, 1330 (Fed. Cir. 2019). Having failed to sustain its meritless allegations of literal infringement, no less than three legal bases foreclose SRT from now pivoting to the doctrine of equivalents. Defendants therefore respectfully request leave to move for summary judgment of noninfringement.

Respectfully,

/s/ Jeremy A. Tigan

Jeremy A. Tigan (#5239)

JAT:lo
Enclosure
cc: All Counsel of Record (via CM/ECF and e-mail)